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established the exon/intron structure of this gene and undertook SSCP analysis of breast tumors. No gene-inactivating mutations were found excluding this gene from involvement in

at the limit of the region suggesting that it was possibly the target for LOH. We

breast cancer development.

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#### **INTRODUCTION:**

Loss of hetereozygosity (LOH) is a mechanism which has been identified in virtually all tumor types analyzed. The molecular assay reveals areas of the genome which have lost one copy of a particular region of a chromosome. It is considered a method by which tumor cells lose the copy of a normal gene but retain a defective copy thus exposing a recessive mutation in a critical gene. LOH analysis of breast cancer has shown that over 50% of tumors lose genetic material from the short arm of chromosome 1, centered on the 1p31 region. We have previously defined a 1.5 Mbp region in 1p31 which is consistently lost in the majority of reported cases where this region was investigated. With the sequencing of the human genome and the availability of genetic annotations of this region which describe the genes located there we have been undertaking a mutation screen in breast tumors of candidate genes. We have excluded the TTC4 gene and the progesterone receptor gene both of which were excellent candidates since they were expressed in normal breast tissue and located within the frequently deleted region. These experiments were completed in the second year and the subject of previous reports.

#### **BODY:**

In October 2000 the P.I. accepted the position of Chair of Cancer Genetics at Roswell Park Cancer Institute and moved his laboratory there in November 2000. The USAMRMC was informed of this change of institution at that time and the paperwork to transfer the grant funding was submitted at the beginning of 2001. As of the 30<sup>th</sup> of September 2001 this transfer has still not taken place and no assurances that it will be completed could be obtained. As a consequence we have been unable to pursue any of the experimental objectives outlined in the statement of work for the final year of this grant. The outstanding tasks therefore remain as they did at the end of the second year.

Task 1:	Completed
Task 2:	Completed

Task 3: Deleted - with the progress of the genome sequencing project this task

became redundant.

Task 4: Completed Task 5: Completed Task 6: In progress

Task 7: Deleted - with the progress of the genome sequencing project this task

became redundant.

The search for the critical 1p31 gene is now relatively straightforward since there are a number of candidate genes in the region which have been identified as a result of the generation of the human genome sequence. We have searched the Public databases and the Celera database to identify genes as well as define their exon/intron structure. We are now poised to undertake mutation analyses as described in the original application which is dependent on the transfer of the remaining funding for the project to hire personnel who will be dedicated to this task.

# **KEY RESEARCH ACCOMPLISHMENTS:**

No progress due to the non-transfer of funding to the new Institution.

## **REPORTABLE OUTCOMES:**

No progress due to the non-transfer of funding to the new Institution.

## **CONCLUSIONS:**

No progress due to the non-transfer of funding to the new Institution

## **REFERENCES:**

None

# **APPENDICES:**

None